tory infection. These immune complexes, having destroyed the original kidneys, may act in similar manner on the transplanted kidney. Equally possible is the formation of immune complexes to antigens acquired after transplantation. Antigens may be new viral antigens, solubilized transplantation antigens or intracellular renal antigens released by mononuclear cell reaction—the latter being an "auto-immune" disease of the transplanted kidney. Support for this causal mechanism is the high percentage of late failures in transplants from identical twins; ten of 17 patients had recurrent nephritis by the fifth year. These patients, thought not to be at risk from transplant immunity, received no immunosuppression. Results with related donor treated with immunosuppression have better survival, but show similar nephritic lesions on biopsy. What is the best long-term treatment protocol to prevent this late failure? An answer is unavailable. The transplant survival is offered in five- to ten-year projected rates. In all likelihood, the kidneys will not last the lifetime of the individual. This will result in a formidable task to retransplant or dialyze in these cases of graft failure in the near future.

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Specific Immunosuppression— Enhancement or Immunologic Tolerance

Current methods of immunosuppression are general, inhibiting helpful immune reactions as well as the harmful ones associated with rejection. Two immunologic mechanisms for specific immunosuppression have been known for years but never applied to vascularized organ grafts. *Immunological tolerance* may be produced by pretreatment with donor antigen *in utero,* in the perinatal period, or, with some antigens, during adult life. Tolerance is thought to represent the removal of all immunocompetent cells which would recognize the antigen as "foreign." Once tolerance is induced, recipients will accept any graft from the donor. *Enhancement* of graft survival is produced by the passive administration of antibodies to donor antigens at the time of transplantation. In contrast to tolerance, enhanced survival is limited to that specific graft. Transplantation of a second graft from the same donor at a later time will result in unaltered rejection. *Enhancement* may be established actively by immunization of the recipient with donor antigen so that only "enhancing" antibodies are formed. Current immunologic speculation is that both tolerance and active enhancement may actually be manifestations of the same mechanism—an antibody mediated suppression of the immune response. Successful clinical application of this principle is the elimination of hemolytic disease of the newborn due to Rh incompatibility by treatment of Rh negative mothers with anti-Rh_0(D) immune globulin.

Kidney transplants exchanged between certain strains of rats will survive indefinitely if treated only four times with enhancing antibody. Control animals die within two weeks. As early as 24 hours after simultaneous grafting and treatment with anti-donor globulin, donor antigens disappear from the endothelial surface of the renal vessels. Three explanations are possible: (1) Enhancing antibody damages endothelial cells in such a fashion that they are replaced by host endothelium. (2) Alternatively, enhancing antibody coats endothelial antigens, preventing their recognition as foreign by host cells. (3) The enhancing antibody may combine with transplantation antigens and remove them from the cell surface. Clinical application of enhancing antibodies (human anti-human transplantation antigen) is awaiting development of purification of the human transplantation antigens, chemical separation of enhancing from cytotoxic antibodies and immunization schedules to achieve high protective-cytotoxic ratios. Investigations along these lines offer the best hope for immunosuppression specific to the donor antigen.

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